STATEMENT UNDER ARTICLE 19(a)

The current application ("PCT-00731") demonstrates a method of characterizing glycosaminoglycans-derived oligosaccharides ("MPS biomarkers") to diagnose, evaluate, and monitor mucopolysaccharidoses ("MPS") patients. The claimed method is useful for diagnosing a pre-clinical-, or clinical-, status of an MPS disease in a target animal. The method comprises determining a target quantity of a target MPS biomarker from a target biological sample taken from the target animal; and comparing the target quantity to a reference quantity of a reference MPS biomarker. The target MPS biomarker is the same as, or equivalent to, the reference MPS biomarker, and each of the target MPS biomarker and the reference MPS biomarker is an oligosaccharide derived from glycosaminoglycans.

In contrast, the references cited by the search report neither recite nor imply the combination of steps of the claimed invention that can be used as a clinical indication of the MPS disease, an indication of a progression of the MPS disease, or an indication of a regression of the MPS disease, as shown by the checked and blank columns in Table 1 (the blank columns indicate no such teaching or suggestion).

The Ramsay et al., 2003 is concerned only with sulphated monosaccharides and one monosuphated disaccharide. This paper does not predict the additional oligosaccharides identified in the MPS or their use as MPS biomarkers. Furthermore, this paper was not listed in the above Table 1 because it is was published after the claimed priority date.

Although the Byers (1998) paper contains a similar element as the current invention, there is a great difference in the detail and characterization of the MPS oligosaccharides biomarkers. For example, the use of mass spectrometry of this invention allows a much greater specificity of the oligosaccharide structures that can be identified as arising from dermatan or heparan sulfate. The identification of the structure also identifies these oligosaccharides as a primary storage products that result directly from the enzyme deficiency. Such detailed characterization translates into a definitive diagnosis and monitoring biomarkers.

Table 1 **Features of a method for diagnosing MPS disease in a target animal.**	Determining a Target Quantity of an MPS Oligosaccharide Biomarker Derived from Glycoasminoglycand (1)	Comparing a Target Oligosaccharide Biomarker to a Reference Oligosaccharide Biomarker (2)	Using a Mass Spectrometric Analysis, an Immuno Assay, Liquid Chromatography, Anion Exchange Chromatography, or Combination thereof; to Determine the Target Quantity and the Reference Quantity of Oligosaccharide MPS Biomarkers (3)
Current Invention	√	√	√
Articles			
Rozaklis (2002)			
Pitt (1997)			
Hopwood (1982)			
Byers (1998)	√		
Hopwood (1998)			
Desaire (2000)			
Sweetman (2001)			
Packer (1998)			
Gerber (2001)			
Fluharty (1982)			
Whitefield (2000)			
Patents			
RU 2 196,988 C2			
WO 03/048784 A2			
WO 01/94941 A2			